STRUCTURE OF BILAYER-WATER AND MONOLAYER-WATER INTERFACES: A MOLECULAR DYNAMICS STUDY

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ABSTRACT

We present large-scale molecular dynamics simulations of interfaces between water and bilayers or monolayers of glycerol monooleate. Good agreement between the calculated structural parameters of the bilayer and the corresponding experimental measurements indicate that our description of systems is realistic at a molecular level. We show that (a) water markedly penetrates the headgroup region but not the hydrocarbon core of the amphiphilic phase, (b) water penetration increases with decreasing density of the headgroups at the surface, (c) the width of the water interfacial region in contact with monolayers is the largest at an intermediate headgroup surface coverage, and (d) water molecules at the interface are polarized such that their excess dipole moment points toward the liquid.

Introduction

The interfaces between cell membranes and water form a unique biological microenvironment in which polar and nonpolar media exist in direct proximity. A large number of essential cellular processes occur in this microenvironment. The selectivity and dynamics of these processes, as well as the conformation and organization of participating molecules are largely determined by the structural and electrical properties of the interface.

It has long been recognized that water is organized differently at the interface with amphiphilic molecules than in the bulk. This ordering may, in turn, contribute to the membrane surface potential and influence the transport of polar and ionic species across the membrane. It has been further proposed that the surface potential correlates with the exponentially decaying hydration force acting between two membrane surfaces.[1] It has also been suggested that water penetration into defects in the membrane surface, caused by molecular-scale fluctuations of the interface, would account for the high permeability of membranes to water and protons.[2] However, experimental tests of these ideas are usually difficult and indirect.

In this paper we directly address the issue mentioned above by presenting results of molecular dynamics simulations of the interface between water and a membrane composed of glycerol 1-monooleate (GMO). The GMO headgroup is polar, but not charged, and the alkyl chain contains 18 carbon atoms with a *cis* double bond between C(9) and C(10). GMO was chosen as the membrane component for reasons of computational and experimental convenience. GMO forms monolayers and stable planar bilayers whose properties can be conveniently studied in laboratory experiments. In addition, by selecting amphiphiles with uncharged head groups, we avoid complications associated with explicitly considering counterions in the calculations.

In experimental studies important information about the state of interfacial water is convenentionally obtained by investigating monolayers at different densities on the water surface. Thus, we also included these systems in our present work.

Methods

The bilayer-water system consisted of 72 GMO molecules arranged in a planar bilayer perpendicular to the z-coordinate of the simulation box and located between two lamellae of water, each containing 1152 molecules. This corresponds to about 10 water layers per lamella. Thus, the system contained two membrane-water interfaces and two free water surfaces. The x,y dimensions of the simulation box were 36.94×36.94 Å to match the experimental surface coverage of 37.9 Å per GMO molecule.[3,4] Four separate molecular dynamics (MD) trajectories at 300 K were obtained for the system, starting from very different initial arrangements of the bilayer. The length of each trajectory was at least 1 ns, after equilibration for about 0.3 ns. Since the statistical averages obtained from these four runs were quite similar, we infer that the system was properly equilibrated.

The monolayer-water system consisted of GMO monolayers spread on both surfaces of a water lamella. The size of the simulation box and the temperature were the same as in the bilayer system. Three densities of amphiphilic molecules were studied- 36, 30 and 18 GMO molecules per surface. This yielded surface coverages of 37.9, 45.5 and 75.8 Å² per molecule, respectively. This water lamella contained 1159 molecules in all three calculations. To investigate systems with higher densities of glycerol at the water surface, we studied glycerol monopalmitate (GMP) on water. GMP, composed of the glycerol headgroup attached to a saturated alkyl chain of 16 carbon atoms, forms monolayers with surface coverage of 22.5 Å² per molecule.[4] For each monolayer-water system, a 1 ns trajectory was obtained after equilibration.

All methyl and methylene groups in the alkyl tails were modeled as uncharged "united atoms", which interact with other atoms via the Lennard-Jones potentials of Jorgensen.[5] All atoms of the headgroup were explicitly considered. The partial charges and potential function parameters of these atoms were based on quantum mechanical calculations on glycerol and ethylene glycol.[6] Further information on methodology is given elsewhere.[6]
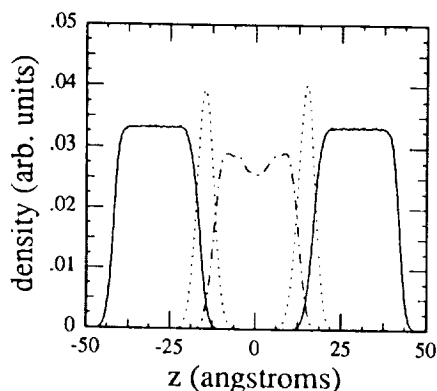

Fig. 1 Density distribution of the water (solid), GMO head groups (dotted) and alkyl chains (dash-dot) as function of z-coordinate perpendicular to the interfaces.
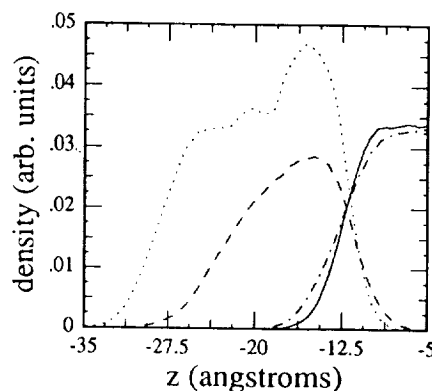
Fig. 2 Density distributions of the water (solid, dash-dot) and GMO atoms (dotted, dashed) in monolayer coverages of 37.9 and 75.8 Å² / molecule, respectively.

Results and Discussion

A. Structure of the Bilayer and the Monolayers

The density distributions of different components of the water-bilayer system are shown in Fig.1. The bilayer was stable and spanned about 35 Å. All polar headgroups were located in two narrow regions at the interfaces with water. The nonpolar hydrocarbon core of the membrane was 27 Å wide, in very good agreement with experimental data.[3] The core was quite fluid with chain disorder increasing towards the center of the bilayer. This fluidity of the GMO tails is responsible for density decrease in the middle of the bilayer. The same effect has also been noticed in recent diffraction experiments.[7]

Very similar density distributions were found for a GMO monolayer on water at the same headgroup density as in the bilayer. As depicted in Fig. 2, these distributions are broader at the lower headgroup density, and the monolayer remained fluid at all surface densities. In contrast, a highly dense monolayer of GMP was well ordered, in agreement with experimental data.[4]

B. Structure of Water at the Interface

As can be seen from Fig. 1, there is a significant amount of water penetration into the head group region of the bilayer, but very little water penetration into the hydrophobic core. Both O-H groups of GMO are extensively hydrated, and there is also some specific hydration of the carbonyl group located a few angstroms deeper in the bilayer. The corresponding water-GMO radial distribution functions (RDFs) are shown in Fig. 3. The degree of water penetration into amphiphilic phase is a function of the surface density of headgroups. As the surface density increases, the average number of water molecules penetrating the monolayers per unit area (defined as those molecules located deeper than the plane which cuts the number density profile of the amphiphiles at half-maximum) decreases from 0.27 to 0.18, 0.16 and 0.14 H_2O / $Å^2$ as the surface coverage decreases from 75.8, to 45.5, 37.9 and 22.5 $GMO/Å^2$, respectively. This indicates that water molecules are partially expelled from the hydrophilic headgroup region and favorable water-glycerol contacts are substituted in part by glycerol-glycerol interactions. By comparing the water density profiles at the interface with GMO at two coverages, shown in Fig. 2, and the pure liquid-vapor interface (see Fig. 1), we note an important structural feature of the interface. The width of the water interface is broader at the lower GMO surface density than at the higher one. However, at very low surface densities, the width of the interface must narrow again to resemble the pure liquid-vapor interface. Therefore, the width of the water interfacial region is a non-monotonic function of the GMO coverage.

In Fig. 4 we show the polarization (the average excess dipole moment) of water in the direction normal to the surface. Water molecules are clearly organized by the excess surface dipole of the headgroups which is located in the outermost region of the GMO surface and points away from water (measured from the negative to the positive charge). To interact favorably with this dipolar layer, the water molecules which penetrate the headgroup region are oriented such that their dipoles points toward water. The magnitude of this polarization, is about the same as that observed at water liquid-vapor interface.[8] Polarization is not proportional to the headgroup density at the surface - it decreases only slightly when the density is reduced by a factor of 2. A relatively large degree of water polarization indicates that water importantly contributes to the total surface potential. A similar conclusion was reached in recent experimental studies.[9]
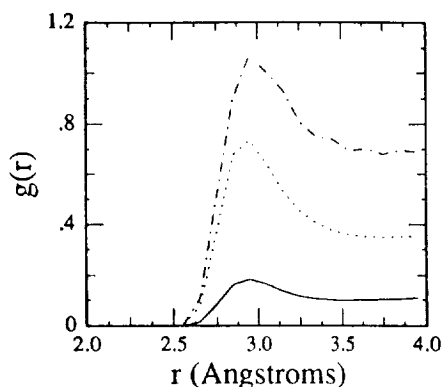
Fig. 3 RDFs for water-GMO carbonyl oxygen (solid) and water-GMO hydroxyl (dotted) fot the bilayer at 37.9 $Å^2$ / molec. The RDF for water-glycerol hydroxyl (dot-dashed) from a single glycerol molecule in water is shown for reference.
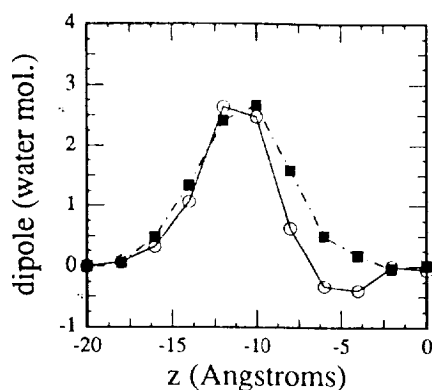
Fig. 4 Water molecular dipole moment for the water-monolayer systems at coverages of 37.9 (open circles) and 75.8 (filled squares) $Å^2$/molec as a function of the distance from the middle of the water lamella.

The water polarization at high headgroup density changes sign in the inner region of the water interface (6-9 Å from the center of the water lamella in the water-monolayer systems). This corresponds to the excess dipole moment pointing toward amphiphiles and, again, yields favorable dipolar water-headgroup interactions. A very similar, non-monotonic behavior of polarization was also observed in MD simulations of a water-phospholipid interface,[10] and led to a conclusion that polarization is not a suitable order parameter for describing hydration forces. Similarly, measurements of ion transport across bilayers indicated that there is no simple correlation between polarization and the hydration force.[9] However, an opposite conclusion was reached in another set of experiments.[1] For lower headgroup densities, the change of sign of polarization is not observed, probably due to the increase interfacial fluctuations.

Finally, it should be mentioned that the existence of excess surface dipole moment of water is not indicative of a high level of "order" of water at the interface. In fact, the orientational distributions of interfacial water are quite broad. A detailed analysis of the structure of the water-bilayer interface can be found elsewhere.[6]

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